

Proper hydration in contrast-induced nephropathy among patients with acute myocardial infarction and cardiac insufficiency

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Abstract

Backgrounds The recommended strategy to prevent contrast-induced nephropathy (CIN) among acute myocardial infarction (AMI) patients is adequate hydration. However, it is still controversial whether adequate hydration should be used to prevent CIN in AMI patients with Killip class>I.

Methods In this prospective, observational registry study, 407 acute myocardial infarction (AMI) patients with Killip class>I undergoing percutaneous coronary intervention (PCI) were analyzed. The recommended hydration rate is haved before or after the procedure(0.5 mL/kg/h for Killip class >I). The endpoint was CIN(an absolute increase in serum creatinine of ≥ 0.5 mg/dL or a relative increase of $\geq 25\%$ within 48-72 hours).Patients were divided into 2 groups by approximate median hydration volumn(HV)750ml. Multivariable logistic regression analysis was carried out to clarify the independent predictors of CIN and worsening heart failure(WHF).

Results The total incidence of CIN was 24.6% in this study. There was a significant association between hydration volume and CIN in two hydration groups(HV >750 mL vs. HV= \leq 750mL: 28.46% vs. 18.18%, $P=0.020$), the WHF(16.2% vs 5.19%, $P=0.001$). After adjusting for confounders, multivariate analysis showed that higher HV was significantly associated with CIN(adjusted odds ratio(OR)=1.829, 95% confidence interval (CI) (1.046, 3.197),) and WHF risk(adjusted OR= 2.585, 95% CI (1.104,6.055)), all P value<0.05.

Conclusions For AMI patients with Killip class>I, relatively adequate hydration(HV>750ml)may be associated with a higher risk of CIN and WHF.

Background

The incidence of contrast-induced nephropathy (CIN) in patients undergoing PCI is about 2% to 25%[1–3]. The incidence of CIN is often higher in patients with acute myocardial infarction (AMI) due to the frequent hemodynamic compromise and the lack of sufficient time for adequate hydration therapy[4–7]. Some studies showed that compared with patients without CIN, CIN increased the risk of adverse cardiovascular events and mortality after PCI with even relatively stable hemodynamics after a 1-year follow-up[8–10]. Recommended strategies to prevent CIN include adequate hydration, usage of low osmolar contrast media and a high-dose statin. Hydration speed should be halved (0.5ml/kg/h) if left ventricular ejection fraction (LVEF) $<35\%$ or Killip class>I[11].

Several studies with small sample size have explored hydration strategies in patients with AMI[9,12–14]. But the agents, timing, quantity of hydration have not been investigated in patients with cardiac insufficiency, especially in AMI patients with Killip class>I. In addition, the efficacy of adequate hydration in preventing CIN and avoiding worsening heart failure was lacking in convinced evidence. The purpose of this study was to evaluate the relationship between adequate hydration and incidence of CIN and WHF among AMI patients with Killip class >I.

Methods

Study Population

This prospective observational study was conducted at Guangdong Provincial People's Hospital between April 2009 to December 2013. We enrolled all consecutive patients with AMI aged more than 18 years old. Eligible participants should be assigned to Killip class>I by physicians. According to our institute protocol, exclusion criteria included malignancy, cardiovascular surgery or endovascular repair, end-stage renal disease or renal replacement and pregnant. The Ethics Committee of Guangdong Provincial People's Hospital approved the study, and all patients gave written informed consent.

PCI Procedure

Cardiac catheterization was performed according to standard clinical practice. Contrast volume was left to the discretion of the interventional cardiologist. Patients would receive isotonic saline intravenously at a rate of 0.5 mL/kg 12h before or 12–24h after the contrast exposure due to Killip class>I. The standard post-PCI therapy consisted of lipid-lowering agents, β -blockers, angiotensin-converting enzyme inhibitors, aspirin, and clopidogrel, based on interventional guidelines.

Data Collection and definition

Serum creatinine measurement at admission before coronary angiography and a subsequent measurement within 7 days after the procedure were required.

Creatinine clearance was calculated by the Modification of Diet in Renal Disease formula [MDRD]. The primary endpoint was the occurrence of CIN, which was defined as an increase in serum creatinine of ≥ 0.5 mg/dL or $\geq 25\%$ from baseline within 48 h of contrast exposure. The second endpoint was WHF, which was diagnosed by at least one clinical evidence of heart failure, including the increasing need for intravenous therapy (inotrope or vasodilator) or mechanical support, new radiologic evidence of pulmonary edema during the index hospitalization by clinicians. A baseline eGFR ≥ 90 mL/min/1.73m² was defined as chronic kidney disease [CKD]. Killip grading was evaluated by physicians.

Statistical Analysis

Patients were divided into 2 groups by 750ml due to the median of hydration volume [700ml] and consideration of the general liquid package [250ml]. Continuous variables were presented as mean \pm standard deviation and independent sample t-tests were performed for normally distributed data. The Wilcoxon rank-sum test was used for 2 groups that did not satisfy a normal distribution. Fisher's exact test or Pearson's chi-square test were used for categorical data, which were expressed as percentages and frequencies. Univariate analysis and multivariate logistic regression models involving stepwise selection

and backward elimination were used to identify the predictors of CIN and WHF. A 2-sided p-value <0.05 was considered significant for all analyses. All data analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Baseline Characteristics

A total of 407 AMI patients with Killip>I class (34.1% female) were included in the final analysis. There was a significant association between HV and the incidence of CIN (HV >750 mL vs. HV = <750mL: 28.46% vs. 18.18%, respectively) and the WHF (16.2% vs 5.19%, respectively) (all *P-trend* < 0.05) (Table 2).

The patients in the HV > 750 mL group were significantly older, had poorer renal function and higher N-terminal pro-brain natriuretic peptide (NT-proBNP) levels. They were more likely to have more hypotensive status and higher Mehran risk scores, and more frequently required diuretics (Table 1). In addition, contrast volume-to-estimated glomerular filtration rate (CV/eGFR) was statistically significant difference.

However, contrast volume was not significantly different in two groups (129.4±51.13 vs 136.7±58.05, *P* = 0.22). There were no statistically significant differences in diabetes mellitus and anemia.

Associations Between Hydration Volume and In-Hospital Outcomes

There was statistically significant difference between hydration volume and CIN in two hydration groups (HV >750 mL vs. HV = <750mL: 28.46% vs. 18.18%, *P* = 0.020), the same tendency was found in the WHF (16.2% vs 5.19%, *P* = 0.001). The patients in the higher HV group showed higher rate of in-hospital death than the lower HV group (6.72% vs 1.95%, *P* = 0.031). However, dialysis rates were similar between the two groups. (Table 2).

Logistic regression analysis for association between HV > 750ml and CIN and WHF

Multivariate logistic regression analysis demonstrated that after adjusting 7 confounders including age>75, diabetes, hypotension, anemia, eGFR<60, LVEF<40% and female, multivariate analysis showed that higher HV was significantly associated with CIN (adjusted OR = 1.83, 95% CI 1.05–3.20, *P* = 0.034) (Figure 1). Female was also an independent risk factor for CIN (adjusted OR = 1.84, 95% CI: 1.009–3.371, *P* = 0.047). Similarly, age>75 and LVEF<40% was also independent risk factors in the multivariate model. In the other multivariate model for WHF, after adjusting 7 confounders, multivariate logistic regression

analysis revealed that the higher HV>750ml was associated with an increased risk of WHF risk (adjusted OR = 2.59, 95% CI:1.10–6.06, $p = 0.029$) [Figure 2]

Discussion

The present study explored the effective and safe hydration volume for the prevention of CIN after CAG or PCI among AMI patients with cardiac insufficiency. Multivariate logistic regression showed that in AMI patients with Killip class>I, hydration volume >750ml at routine speed was not statistically associated with reducing the incidence of CIN, but an independent risk factor for WHF.

Several previous studies have explored the optimal hydration strategy [15–17], but the guidelines for patients with cardiac insufficiency still don't have specific hydration strategy recommendation, especially in patients with cardiac insufficiency [18]. The recommended prevention for CIN was routine hydration 12 hour before and 6–24 hour after the procedure with saline at regular speed (1 ml/kg/h or 0.5ml/kg/h for patients with NYHA>II or LVEF<35%). Hydration strategy was used to be normalized by weight. However, most patients with primary PCI were not likely to obtain their weight and monitor their creatine before the contrast exposure. Fluid overload plays an important role in the pathogenesis of WHF and leads to prolonged hospitalization [19,20]. Therefore, AMI patients with Killip>I should get a targeted treatment to prevent CIN and to avoid fluid overload.

The incidence of CIN was much higher in our study when compared with other clinical trials of patients with acute coronary syndrome [9,21,22]. The mehran score

in two groups were both recognised as the middle risk. But their cardiac function have contributed to the high incidence of CIN and WHF. Maioli et al [17] assigned 450 STEMI patients to receive preprocedural and postprocedural hydration of isotonic saline or sodium bicarbonate. Their study suggested that adequate hydration may prevent CIN in patients undergoing primary PCI and hydration volume <960 mL was one of the independent predictors of CIN. The result was contrary to ours. The hydration agents in the 2 groups were sodium bicarbonate and saline. Meanwhile the proportion of patients with Killip>I was less than 25% in 3 groups. Many studies have demonstrated that furosemide with matched hydration by the RenalGuard System seems to reduce the incidence of CIN [4,23–25]. The hydration volume was $3,995 \pm 1,401$ ml and $1,742 \pm 290$ ml in the Renalguard and control group, respectively. The RenalGuard system matching with furosemide could maintain a high urine output [>300 ml/h] during the procedure and improve simultaneously renal medulla perfusion. However, All patients with symptoms of acute heart failure were excluded. And the device was so expensive and inconvenient that the clinical application was not feasible. Some expert opinion of prevention of AKI suggested that hydration volumes above 11 ml/kg were associated with continuously increased rates of AKI in patients with chronic kidney disease (CKD) [26]. Study by Chen et al illustrated that hydration volumes greater than 15 ml/kg at routine speed may be associated with risk of CIN in patients with advanced congestive heart failure undergoing PCI [27], consistent with our understanding of the hydration volume in cardiac insufficiency.

Fluid overload could increase intraventricular pressure, myocardial stretching, and neurohormonal activation. Excessive hydration may or may not lead to an increase in renal interstitial pressure and oedema, reduction of renal blood flow and local oxygen exchange, and diffuse metabolic dysfunction at the same time[28,29]. This may explain that adequate hydration may not reduce CIN.

Most of the patients in our study might represent a special subtype of Type 1 acute cardiorenal syndrome (CRS), which is defined as acute kidney injury complicating acute heart failure resulting from acute coronary syndrome. The latest statement about CRS [30] from the American Heart Association has mentioned some optimal methods to assess fluid status, such as RenalGuard System, Bioimpedance vector analysis (BIVA), measurement of intra-abdominal pressures (IAP), relative blood volume monitoring devices and so on hopefully. However, whether the non-invasive devices will affect clinical outcomes in patients with HF still remains unknown.

Our studies suggested that the maximum volume was 750ml regardless of the weight of patients in AMI patients with Killip>I. Another clinical implication in our study is that in patients with Killip >I, monitoring urinary output and fluid status might be helpful in earlier detection of renal function.

This study has several limitations. First of all, this single-center study might have been subject to bias although we have adjusted for confounders.

The evidence may not be as strong for its small simple size. Large size of prospective multicenter for hydration strategy in patients with HF are needed. Second, oral hydration volume was lacking. There must be some bias in the final hydration volume.

This study has several limitations. First of all, this single-center study might have been subject to bias although we have adjusted for confounders. The evidence may not be as strong for its small simple size. Large size of prospective multicenter and randomized controlled studies are needed. Second, oral hydration volume were lacking. There must be some bias in the final hydration volume. Third, variation in the measurement times may have led to the missing of postprocedural peak levels of creatinine. Further multicenter, randomized, controlled clinical trials are needed to explore the optimal hydration strategy to prevent CIN.

In conclusion, adequate hydration volume with normal saline at a routine speed may associated with higher risk of CIN and WHF among AMI patients with Killip>I. Device- assisted hydration strategies are expected to evaluate the fluid status and receive individualized hydration

Declarations

Availability of data and materials

The dataset used in the analyses reported here are not publicly available. Access to these data was provided by Yong Liu MD under a limited agreement. Requests to access these de-identified data can

made to Yong Liu MD (liuyong2099@126.com) who will consider the request and may grant reasonable access.

Abbreviations

CIN Contrast-induced nephropathy

AMI Acute myocardial infarction

PCI Percutaneous coronary intervention

HV Hydration volume

WHF Worsening heart failure

LVEF Left ventricular ejection fraction

MDRD Modification of diet in renal disease

CKD Chronic kidney disease

CV/eGFR Contrast volume-to-estimated glomerular filtration rate

BIVA Bioimpedance vector analysis

IAP: Intra-abdominal pressures

AKI Acute kidney injury

CAG Coronary angiography

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Ethics declarations

Ethics approval

This study was approved by the ethical review committee of Guangdong Provincial People's Hospital

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1. Comparison of baseline results in 407 patients

Variables	HV ≤750 mL	HV>750 mL	p-value
Number	154	253	
Demographics			
Age (y)	63.37±11.40	66.81±10.66	0.002
Age >75 y	30±19.48	69±27.27	0.075
Female	34±22.08	48±18.97	0.449
Weight (kg)	64.42±11.36	63.63±10.26	0.467
Heart rate	78.64±15.75	81.35±19.73	0.150
Hypertension	77±50.00	148±58.73	0.086
Diabetes mellitus	45±29.22	64±25.30	0.386
Anemia	63±41.18	95±38.00	0.526
Hyperlipidaemia	18±11.69	28±11.07	0.848
Previous MI	3±1.95	16±6.32	0.042
Examination			
SBP, mmHg			
eGFR, mL/min/1.73 m ²	72.38±28.83	56.76±25.66	<.0001
SCr, mg/dl	92.31±44.24	113.8±48.27	<.0001
BUN, mmol/L	5.49±3.42	6.70±4.18	0.003
LVEF	53.07±11.36	50.66±11.54	0.050
Hemoglobin	130.0±17.84	129.2±18.81	0.705
HbA1c	6.64±1.51	6.72±1.63	0.670
NT-proBNP, pg/ml	2928.7±4785.5	5065.7±7991.2	0.016
LDLC, mmol/L	2.77±0.91	2.97±1.05	0.080
Hs-CRP, mg/L	27.29±40.00	38.0576±42.91	0.069
Medication			
Statin	152(98.70)	249(98.42)	0.819
Diuretic	54±35.06	128±50.59	0.002
ACEI/ARB	136±88.31	213±84.19	0.249
Beta-blocker	123±79.87	174±68.77	0.015
Procedure			

characteristics	characteristics		
No of lesion	2.12±1.03	2.37±1.00	0.660
No of stents used	1.62±1.05	1.62±1.05	0.990
Length of stents	42.14±29.17	41.97±28.29	0.960
Contrast volume, mL	129.4±51.13	136.7±58.05	0.220
IABP	1(0.76)	7(3.55)	0.152
CV/eGFR	2.18±1.51	2.93±1.89	<.0001
Mehran-Score	8.88±3.95	10.33±5.10	0.002
Hypotension	5[3.25]	32[12.70]	0.001

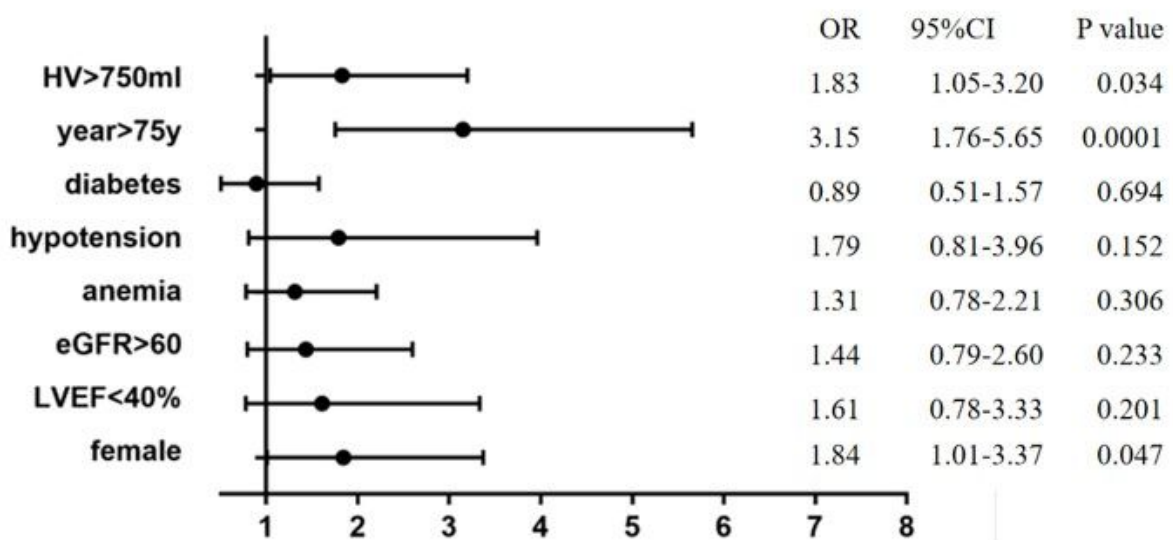
Abbreviations: SBP: systolic blood pressure; CHF: congestive heart failure; MI: myocardial infarction; SCr: serum creatinine; eGFR: estimated glomerular filtration rate; NT-proBNP: N-terminal pro-brain natriuretic peptide; LVEF: left ventricular ejection fraction; LDL: low density lipoprotein; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CM: contrast medium; HV: hydration volume/ weight; CV[Contrast Volume; Hs-CRP: high-sensitivity C-reactive protein; HCT: haematocrit

Table 2. Incidence of in-hospital events

Variables	HV≤750 mL/kg	HV>750mL	p-value
CIN, n(%)	28[18.18]	72[28.46]	0.020
WHF, n(%)	8(5.19)	41(16.2)	0.009
Dialysis, n(%)	5[3.25]	11[4.35]	0.579
Stroke, n(%)	2(1.30)	5(1.98)	0.610
Death, n(%)	3(1.95)	17(6.72)	0.031

Abbreviations: CIN: contrast-induced nephropathy ;WHF:worsening heart failure

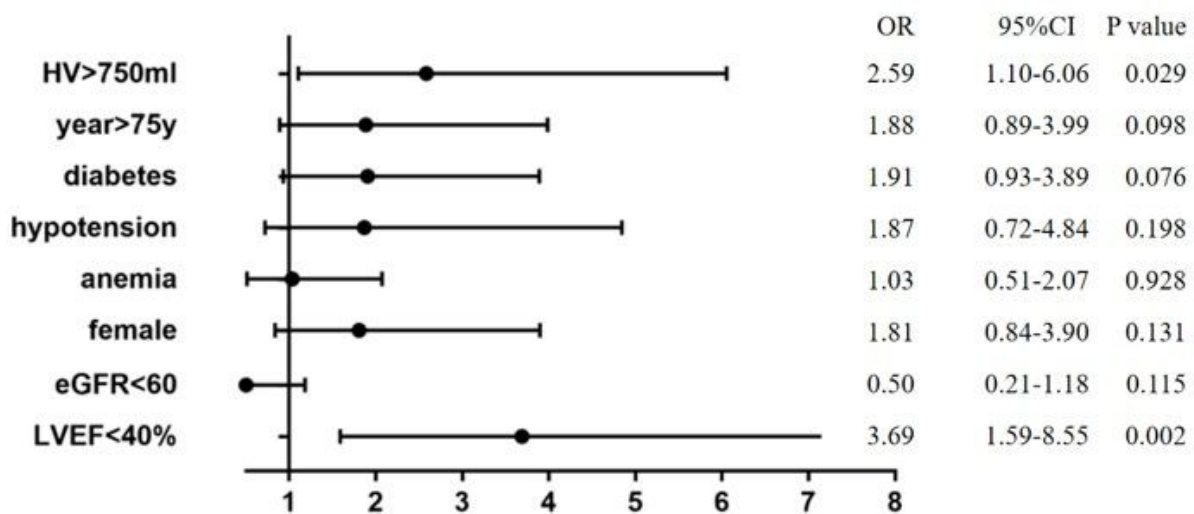
Figures



Abbreviations: HV:hydration volume

Figure 1

Multivariate logistic regression analysis for the association between CIN and HV >750ml



Abbreviations: HV:hydration volume

Figure 2

